

Autoimmune hepatitis

Autoimmune hepatitis is a disease in which the body's own immune system attacks the liver and causes it to become inflamed.

?Clinical Presentation:

- Before a diagnosis of autoimmune hepatitis can be made, it is important to exclude other causes: toxic (alcohol, drugs)
 - metabolic diseases (Wilson's disease, haemochromatosis, A1-antitrypsin deficiency), hepatitis and HCV. viral causes, although there is a complex link between autoimmune
- .Predominantly a disease of younger women (90% of patients are female).
- May present with acute hepatitis, jaundice, profound malaise and fatigue, and amenorrhoea in women (?autoimmune).
 - May be marked extra-hepatic features: vitiligo and alopecia, thyroid disease, pernicious anaemia, type I diabetes mellitus, autoimmune haemolytic anaemia and ITP, rheumatoid arthritis, ulcerative colitis, glomerulonephritis, cryptogenic ?broising alveolitis, and coeliac disease.

?Immunogenetics

- There is a strong association with HLA-B1, B8, DR3, DR4.

?Immunopathology

Major features are piecemeal necrosis of hepatocytes in the periportal region.

- There is an infiltrate of CD4+ T cells and B cells.
- Later stages of the disease show typical cirrhosis.

?Diagnosis?

- LFTs show markedly elevated transaminases.
- Prothrombin time may be prolonged in late disease.
- Markers of hepatitis virus infection are absent.
- Polyclonal hypergammaglobulinaemia (mainly IgG and IgA).

?Autoantibodies

- Antibodies to HCV or HCV PCR+ = exclusion criteria for autoimmune hepatitis!

- addition to the LKM antibodies.

Type 2b hepatitis is associated with antibodies to hepatitis C in

- Autoantibodies to nuclear components, dsDNA, smooth muscle (anti-actin), LKM antibodies, and liver membranes can be detected.

- Low-titre AMA may also be detected.

The pattern of antibodies present has led to a classification scheme for autoimmune hepatitis.

- Autoimmune hepatitis type 1 (AIH-1) is ANA+, smooth muscle antibody (SMA)+, P-ANCA+, and soluble liver antigen (SLA) antibody+.

In AIH-1, 50% are ANA

- +/SMA+, 15% are ANA+ only, and 35% are SMA+ only.

- + only. 8% of AIH-1 are SLA

- to therapy; 90% female.

Typically occurs in adults, has a better prognosis, and responds well.

- Previously known as lupoid hepatitis. High frequency of extrahepatic features.

- Autoimmune hepatitis type 2a (AIH-2a) is typically liver–kidney microsomal (LKM-1, LKM-3) antibody+ and liver cytosol (LC-1) antibody+.

- + only. 43% of AIH-2 are LC-1 with poor response to therapy.

AIH-2a is seen in children (50% of cases) and has a worse prognosis

- Hypergammaglobulinaemia is less marked; IgA is usually low. Associated with thyroid and gastric parietal cell autoimmunity.

- Autoimmune hepatitis type 2b (AIH-2b).

- No female predominance; occurs in over-40s; milder disease. HCV-associated; HCV-RNA positive, antibodies to HCV positive.

- No extra-hepatic features.

- LKM-1 positive (NB: HCV antigen cross-reactive with P450 (IID6)

- cytochrome).

- Autoimmune hepatitis type 3 (AIH-3) is ANA–, LKM–, SLA+. SMA and AMA are seen less commonly.

- that of type 1. Most patients are women (90%) and have a similar presentation to

- Autoimmune hepatitis type 4 (AIH-4).

- with antibodies to M2 antigen. Overlap syndrome of autoimmune hepatitis and PBC; AMA positive

- There are cases of biopsy-proven but serologically negative hepatitis.

- Tests for both SLA and LC-1 should be performed.

- LKM-1 antibodies recognize the cytochrome P450IID6 and are associated with types 2a and 2b autoimmune chronic active hepatitis.

?Other autoantibodies in hepatitis

- Liver–kidney microsomal antibodies may be found in autoimmune hepatitis and recognize different hepatic cytochrome enzymes.

?LKM-1: cytochrome P450 (IID6). associated with types 2a and 2b autoimmune hepatitis. Antibodies to LKM-1 may be triggered by HCV and HSV as both have proteins sharing homology with P450 (IID6). France only.

?LKM-2: cytochrome P450 (IIC9). Drug-induced, tienilic acid, in antibod